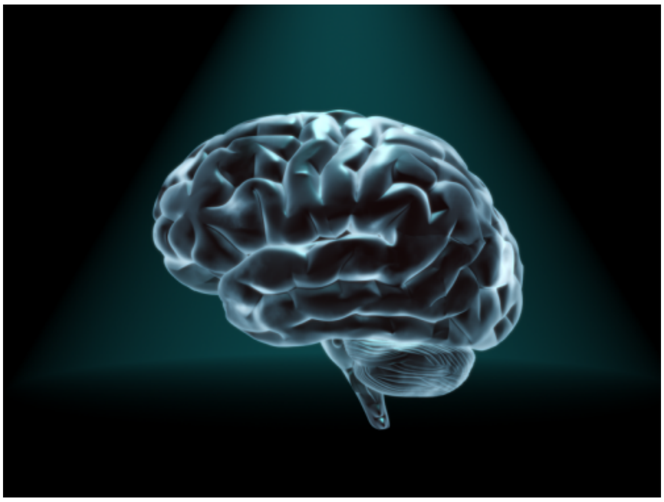
How does manganese enter the brain? Research offers clues to neurological disorder

27 August 2018, by Ellen Goldbaum



Credit: Human Brain Project

New information from the University at Buffalo on how manganese, an essential nutrient, gets into the brain, is helping shed light on a neurological disorder usually associated with industrial overexposure to the metal.

In June, Brittany Steimle, a doctoral candidate in biochemistry at UB, received the award for outstanding poster for her presentation on how proteins transport manganese in the brain at the international "Trace Elements in Biology and Medicine" conference, sponsored by the Federation of American Societies for Experimental Biology in Tahoe City, California.

Steimle conducts research in the laboratory of Daniel J. Kosman, Ph.D., SUNY Distinguished Professor in the Department of Biochemistry in the Jacobs School of Medicine and Biomedical Sciences at UB, where the focus is on the regulation of manganese and other essential nutrients in the brain.

She explained that manganese is essential for bone formation, brain development and metabolizing carbohydrates, cholesterol and amino acids.

However, she noted, workers in the welding, mining and ore-crushing industries may be susceptible to overexposure by inhaling manganese, which can induce neurological disorders like manganism, a condition that resembles Parkinson's disease with symptoms like tremors, difficulty walking and facial spasms. The similarity between the two has led to proposals that manganese may also play a role in Parkinson's disease.

"To develop therapeutics for manganese-induced neurological diseases, we must first understand how manganese enters the brain," said Steimle.

Her study focused on how dietary manganese crosses into the brain through the blood-brain barrier, (BBB), an impermeable barrier that regulates passage of nutrients into the brain. Brain microvascular endothelial cells make up the basis of the BBB through the formation of tight junctions between endothelial cells.

"Due to the restrictive nature of this barrier, nutrients can only pass into the brain through transporters and chaperone proteins expressed by these endothelial cells," she said. "Our objective is to characterize the transport systems that regulate manganese uptake into the brain and to further investigate how such mechanisms protect against manganese-induced neurotoxicity."

In Kosman's lab, Steimle and her colleagues do this using an in vitro model of the BBB, developed by Ryan McCarthy, Ph.D., previously a graduate student in the lab. In the model, the brain microvascular endothelial cells are grown under conditions that imitate the in vivo environment of the BBB.

"Understanding how manganese accumulates into the brain through the blood-brain barrier may serve as a key to designing drug targets for individuals who may have been overexposed to manganese in the environment or in whom manganese metabolism has somehow become dysregulated," she said.

Provided by University at Buffalo

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